



RECEIVED
JUN 16 2003
TECH CENTER 1600/2900

1

SEQUENCE LISTING

<110> TSCHOPP, JURG

<120> APRIL-A NOVEL PROTEIN WITH GROWTH EFFECTS

<130> A049 US

<140> 09/520,489

<141> 2000-03-08

<150> PCT/US98/19191

<151> 1998-09-11

<150> 60/079,384

<151> 1998-03-26

<150> 60/058,786

<151> 1997-09-12

<160> 16

<170> PatentIn Ver. 2.1

<210> 1

<211> 1346

<212> DNA

<213> Homo sapiens

<400> 1

ggtagcaggc ttcttagagg gactggaacc taattctcct gaggtcgagg gaggggtggag 60
gggtctcaagg caacgctggc cccacgacgg agtgccagga gcactaacag tacccttagc 120
ttgctttcct cctccctcct ttttattttc aagttccttt ttatttctcc ttgcgtaaca 180
acctttctcc cttctgcacc actgcccgtg cctttaaccg ccccgccacc tccttgctac 240
cccactcttg aaaccacagc tgttggcagg gtccccagct catgccagcc tcattctcctt 300
tcttgctagc ccccaaaggg cctccaggca acatgggggg cccagtcaga gagccggcac 360
tctcagttgc cctctggttg agttgggggg cagctctggg ggccgtggct tgtgccatgg 420
ctctgctgac ccaacaaaca gagctgcaga gcctcaggag agaggtgagc cggctgcagg 480
ggacaggagg cctcccaga atggggaagg gtatccctgg cagagtctcc cggagcagag 540
ttccgatgcc ctggaagcct gggagaatgg ggagagatcc cggaaaaggg agcagtgtctc 600
acccaaaaac agaagaagca gcaactctgtc ctgcacctgg ttcccattaa cgccacctcc 660
aaggatgact ccgatgtgac agaggtgatg tggcaaccag ctcttaggcg tgggagaggc 720
ctacaggccc aaggatatgg tgtccgaatc caggatgctg gagtttatct gctgtatagc 780
cagggtcctgt ttcaagacgt gactttcacc atgggtcagg tgggtgtctg agaaggccaa 840
ggaaggcagg agactctatt ccgatgtata agaagtatgc cctcccaccc ggaccggggc 900
tacaacagct gctatagcgc aggtgtcttc catttacacc aaggggatat tctgagtgtc 960
ataattcccc gggcaagggc gaaacttaac ctctctccac atggaacctt cctgggggtt 1020
gtgaaactgt gattgtgta taaaaagtgg ctcccagctt ggaagaccag ggtgggtaca 1080
tactggagac agccaagagc tgagtatata aaggagaggg aatgtgcagg aacagaggca 1140
tcttctctggg tttggtctcc cgttctctac ttttcccttt tcattccac cccctagact 1200
ttgattttac ggatatcttg cttctgttcc ccatggagct ccgaattctt gcgtgtgtgt 1260
agatgagggg cgggggacgg gcgccaggca ttgttcagac ctggtcgggg cccactggaa 1320
gcatccagaa cagcaccacc atctta 1346

<210> 2

<211> 250

EXPRESS MAIL
EV133111510US

<212> PRT

<213> Homo sapiens

<400> 2

Met Pro Ala Ser Ser Pro Phe Leu Leu Ala Pro Lys Gly Pro Pro Gly
 1 5 10 15
 Asn Met Gly Gly Pro Val Arg Glu Pro Ala Leu Ser Val Ala Leu Trp
 20 25 30
 Leu Ser Trp Gly Ala Ala Leu Gly Ala Val Ala Cys Ala Met Ala Leu
 35 40 45
 Leu Thr Gln Gln Thr Glu Leu Gln Ser Leu Arg Arg Glu Val Ser Arg
 50 55 60
 Leu Gln Gly Thr Gly Gly Pro Ser Gln Asn Gly Glu Gly Tyr Pro Trp
 65 70 75 80
 Gln Ser Leu Pro Glu Gln Ser Ser Asp Ala Leu Glu Ala Trp Glu Asn
 85 90 95
 Gly Glu Arg Ser Arg Lys Arg Arg Ala Val Leu Thr Gln Lys Gln Lys
 100 105 110
 Lys Gln His Ser Val Leu His Leu Val Pro Ile Asn Ala Thr Ser Lys
 115 120 125
 Asp Asp Ser Asp Val Thr Glu Val Met Trp Gln Pro Ala Leu Arg Arg
 130 135 140
 Gly Arg Gly Leu Gln Ala Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala
 145 150 155 160
 Gly Val Tyr Leu Leu Tyr Ser Gln Val Leu Phe Gln Asp Val Thr Phe
 165 170 175
 Thr Met Gly Gln Val Val Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr
 180 185 190
 Leu Phe Arg Cys Ile Arg Ser Met Pro Ser His Pro Asp Arg Ala Tyr
 195 200 205
 Asn Ser Cys Tyr Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile
 210 215 220
 Leu Ser Val Ile Ile Pro Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro
 225 230 235 240
 His Gly Thr Phe Leu Gly Phe Val Lys Leu
 245 250

<210> 3

<211> 917

<212> DNA

<213> Mus sp.

<400> 3

```

gaattcggca cgaggctcca ggccacatgg ggggctcagt cagagagcca gccctttcgg 60
ttgctctttg gttgagttgg ggggcagttc tgggggctgt gacttggtgt gtcgcactac 120
tgatccaaca gacagagctg caaagcctaa ggccgggaggt gagccgggctg cagcgggagtg 180
gagggccttc ccagaagcag ggagagcgcc catggcagag cctctgggag cagagtcctg 240
atgtcctgga agcctggaag gatggggcga aatctcggag aaggagagca gtactcacc 300
agaagcacia gaagaagcac tcagtctctg atcttgttcc agttaacatt acctccaagg 360
actctgacgt gacagaggtg atgtggcaac cagtacttag gcgtgggaga ggccttgagg 420
gcccagggag acattgtacg agtctgggac actggaattt atctgctcta tagtcaggtc 480
ctgtttcatg atgtgacttt cacaatgggt cagggtggtat ctcggaagg acaagggaga 540
agagaaactc tattccgatg tatcagaagt atgccttctg atcctgaccg tgcctacaat 600
agctgctaca gtgcaggtgt ctttcattta catcaagggt atattatcac tgtcaaaatt 660
ccacgggcaa acgcaaaact tagcctttct ccgcatggaa cattcctggg gtttgtgaaa 720
ctatgattgt tataaagggg gtggggattt cccattccaa aaactggcta gacaaaggac 780
aaggaacggt caagaacagc tctccatggc tttgccttga ctgttggtcc tccctttgcc 840
tttcccgcgc ccactatctg ggctttgact ccatggatat taaaaaagta gaattttttg 900
tgtttatctc ccaaaaaa

```

<210> 4

<211> 232

<212> PRT

<213> Mus sp.

<400> 4

E4

```

Met Gly Gly Ser Val Arg Glu Pro Ala Leu Ser Val Ala Leu Trp Leu
  1              5              10              15

Ser Trp Gly Ala Val Leu Gly Ala Val Thr Cys Ala Val Ala Leu Leu
          20              25              30

Ile Gln Gln Thr Glu Leu Gln Ser Leu Arg Arg Glu Val Ser Arg Leu
          35              40              45

Gln Arg Ser Gly Gly Pro Ser Gln Lys Gln Gly Glu Arg Pro Trp Gln
  50              55              60

Ser Leu Trp Glu Gln Ser Pro Asp Val Leu Glu Ala Trp Lys Asp Gly
  65              70              75              80

Ala Lys Ser Arg Arg Arg Arg Ala Val Leu Thr Gln Lys His Lys Lys
          85              90              95

Lys His Ser Val Leu His Leu Val Pro Val Asn Ile Thr Ser Lys Asp
          100              105              110

Ser Asp Val Thr Glu Val Met Trp Gln Pro Val Leu Arg Arg Gly Arg
          115              120              125

Gly Pro Gly Gly Gln Gly Asp Ile Val Arg Val Trp Asp Thr Gly Ile
          130              135              140

Tyr Leu Leu Tyr Ser Gln Val Leu Phe His Asp Val Thr Phe Thr Met
          145              150              155              160

Gly Gln Val Val Ser Arg Glu Gly Gln Gly Arg Arg Glu Thr Leu Phe
          165              170              175

```

Arg Cys Ile Arg Ser Met Pro Ser Asp Pro Asp Arg Ala Tyr Asn Ser
180 185 190

Cys Tyr Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile Ile Thr
195 200 205

Val Lys Ile Pro Arg Ala Asn Ala Lys Leu Ser Leu Ser Pro His Gly
210 215 220

Thr Phe Leu Gly Phe Val Lys Leu
225 230

<210> 5

<211> 233

<212> PRT

<213> Homo sapiens

<400> 5

Met Gly Gly Pro Val Arg Glu Pro Ala Leu Ser Val Ala Leu Trp Leu
1 5 10 15

Ser Trp Gly Ala Ala Leu Gly Ala Val Ala Cys Ala Met Ala Leu Leu
20 25 30

Thr Gln Gln Thr Glu Leu Gln Ser Leu Arg Arg Glu Val Ser Arg Leu
35 40 45

Gln Gly Thr Gly Gly Pro Ser Gln Asn Gly Glu Gly Tyr Pro Trp Gln
50 55 60

Ser Leu Pro Glu Gln Ser Ser Asp Ala Leu Glu Ala Trp Glu Asn Gly
65 70 75 80

Glu Arg Ser Arg Lys Arg Arg Ala Val Leu Thr Gln Lys Gln Lys Lys
85 90 95

Gln His Ser Val Leu His Leu Val Pro Ile Asn Ala Thr Ser Lys Asp
100 105 110

Asp Ser Asp Val Thr Glu Val Met Trp Gln Pro Ala Leu Arg Arg Gly
115 120 125

Arg Gly Leu Gln Ala Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala Gly
130 135 140

Val Tyr Leu Leu Tyr Ser Gln Val Leu Phe Gln Asp Val Thr Phe Thr
145 150 155 160

Met Gly Gln Val Val Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr Leu
165 170 175

Phe Arg Cys Ile Arg Ser Met Pro Ser His Pro Asp Arg Ala Tyr Asn
180 185 190

Ser Cys Tyr Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile Leu
195 200 205

54
ad

Ser Val Ile Ile Pro Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro His
 210 215 220

Gly Thr Phe Leu Gly Phe Val Lys Leu
 225 230

<210> 6
 <211> 134
 <212> PRT
 <213> Homo sapiens

<400> 6
 Val Leu His Leu Val Pro Ile Asn Ala Thr Ser Lys Asp Asp Ser Asp
 1 5 10 15

Val Thr Glu Val Met Trp Gln Pro Ala Leu Arg Arg Gly Arg Gly Leu
 20 25 30

Gln Ala Gln Gly Tyr Gly Val Arg Ile Gln Asp Ala Gly Val Tyr Leu
 35 40 45

Leu Tyr Ser Gln Val Leu Phe Gln Asp Val Thr Phe Thr Met Gly Gln
 50 55 60

Val Val Ser Arg Glu Gly Gln Gly Arg Gln Glu Thr Leu Phe Arg Cys
 65 70 75 80

Ile Arg Ser Met Pro Ser His Pro Asp Arg Ala Tyr Asn Ser Cys Tyr
 85 90 95

Ser Ala Gly Val Phe His Leu His Gln Gly Asp Ile Leu Ser Val Ile
 100 105 110

Ile Pro Arg Ala Arg Ala Lys Leu Asn Leu Ser Pro His Gly Thr Phe
 115 120 125

Leu Gly Phe Val Lys Leu
 130

<210> 7
 <211> 145
 <212> PRT
 <213> Homo sapiens

<400> 7
 Val Ala His Val Val Ala Asn Pro Gln Ala Glu Gly Gln Leu Gln Trp
 1 5 10 15

Leu Asn Arg Arg Ala Asn Ala Leu Leu Ala Asn Gly Val Glu Leu Arg
 20 25 30

Asp Asn Gln Leu Val Val Pro Ser Glu Gly Leu Tyr Leu Ile Tyr Ser
 35 40 45

Gln Val Leu Phe Lys Gly Gln Gly Cys Pro Ser Thr His Val Leu Leu
 50 55 60

E4
 W

Thr His Thr Ile Ser Arg Ile Ala Val Ser Tyr Gln Thr Lys Val Asn
65 70 75 80

Leu Leu Ser Ala Ile Lys Ser Pro Cys Gln Arg Glu Thr Pro Glu Gly
85 90 95

Ala Glu Ala Lys Pro Trp Tyr Glu Pro Ile Tyr Leu Gly Gly Val Phe
100 105 110

Gln Leu Glu Lys Gly Asp Arg Leu Ser Ala Glu Ile Asn Arg Pro Asp
115 120 125

Tyr Leu Asp Phe Ala Glu Ser Gly Gln Val Tyr Phe Gly Ile Ile Ala
130 135 140

Leu
145

<210> 8

<211> 142

<212> PRT

<213> Homo sapiens

<400> 8

Ala Ala His Leu Ile Gly Asp Pro Ser Lys Gln Asn Ser Leu Leu Trp
1 5 10 15

Arg Ala Asn Thr Asp Arg Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser
20 25 30

Asn Asn Ser Leu Leu Val Pro Thr Ser Gly Ile Tyr Phe Val Tyr Ser
35 40 45

Gln Val Val Phe Ser Gly Lys Ala Tyr Ser Pro Lys Ala Thr Ser Ser
50 55 60

Pro Leu Tyr Leu Ala His Glu Val Gln Leu Phe Ser Ser Gln Tyr Pro
65 70 75 80

Phe His Val Pro Leu Leu Ser Ser Gln Lys Met Val Tyr Pro Gly Leu
85 90 95

Gln Glu Pro Trp Leu His Ser Met Tyr His Gly Ala Ala Phe Gln Leu
100 105 110

Thr Gln Gly Asp Gln Leu Ser Thr His Thr Asp Gly Ile Pro His Leu
115 120 125

Val Leu Ser Pro Ser Thr Val Phe Phe Gly Ala Phe Ala Leu
130 135 140

<210> 9

<211> 136

<212> PRT

<213> Homo sapiens

<400> 9

Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu Glu
 1 5 10 15

Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr Lys
 20 25 30

Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr Ser
 35 40 45

Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser His
 50 55 60

Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met Met
 65 70 75 80

Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala Arg
 85 90 95

Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His Leu
 100 105 110

Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser Gln
 115 120 125

Thr Phe Phe Gly Leu Tyr Lys Leu
 130 135

<210> 10

<211> 158

<212> PRT

<213> Homo sapiens

<400> 10

Ala Ala His Ile Thr Gly Thr Arg Gly Arg Ser Asn Thr Leu Ser Ser
 1 5 10 15

Pro Asn Ser Lys Asn Glu Lys Ala Leu Gly Arg Lys Ile Asn Ser Trp
 20 25 30

Glu Ser Ser Arg Ser Gly His Ser Phe Leu Ser Asn Leu His Leu Arg
 35 40 45

Asn Gly Glu Leu Val Ile His Glu Lys Gly Phe Tyr Tyr Ile Tyr Ser
 50 55 60

Gln Thr Tyr Phe Arg Phe Gln Glu Glu Ile Lys Glu Asn Thr Lys Asn
 65 70 75 80

Asp Lys Gln Met Val Gln Tyr Ile Tyr Lys Tyr Thr Ser Tyr Pro Asp
 85 90 95

Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys Trp Ser Lys Asp
 100 105 110

E4
 m

Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly Gly Ile Phe Glu Leu
115 120 125

Lys Glu Asn Asp Arg Ile Phe Val Ser Val Thr Asn Glu His Leu Ile
130 135 140

Asp Met Asp His Glu Ala Ser Phe Phe Gly Ala Phe Leu Val
145 150 155

<210> 11

<211> 141

<212> PRT

<213> Homo sapiens

<400> 11

Ala Ala His Tyr Glu Val His Pro Arg Pro Gly Gln Asp Gly Ala Gln
1 5 10 15

Ala Gly Val Asp Gly Thr Val Ser Gly Trp Glu Lys Ala Arg Ile Asn
20 25 30

Ser Ser Ser Pro Leu Arg Tyr Asn Arg Gln Ile Gly Glu Phe Ile Val
35 40 45

Thr Arg Ala Gly Leu Tyr Tyr Leu Tyr Cys Gln Val His Phe Asp Glu
50 55 60

Gly Lys Ala Val Tyr Leu Lys Leu Asp Leu Leu Val Asp Gly Val Leu
65 70 75 80

Ala Leu Arg Cys Leu Glu Glu Phe Ser Ala Thr Ala Ala Ser Ser Leu
85 90 95

Gly Pro Gln Leu Arg Leu Cys Gln Val Ser Gly Leu Leu Ala Leu Arg
100 105 110

Pro Gly Ser Ser Leu Arg Ile Arg Thr Leu Pro Trp Ala His Leu Lys
115 120 125

Ala Ala Pro Phe Leu Thr Tyr Phe Gly Leu Phe Gln Val
130 135 140

<210> 12

<211> 149

<212> PRT

<213> Homo sapiens

<400> 12

Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro Ser Gly Ser His
1 5 10 15

Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Gly Lys Ile
20 25 30

Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile Val Asn Gln Asp Gly
35 40 45

94

Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser
 50 55 60
 Gly Asp Leu Ala Thr Glu Tyr Leu Gln Leu Met Val Tyr Val Thr Lys
 65 70 75 80
 Thr Ser Ile Lys Ile Pro Ser Ser His Thr Leu Met Lys Gly Gly Ser
 85 90 95
 Thr Lys Tyr Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn
 100 105 110
 Val Gly Gly Phe Phe Lys Leu Arg Ser Gly Glu Glu Ile Ser Ile Glu
 115 120 125
 Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe
 130 135 140
 Gly Ala Phe Lys Val
 145

<210> 13
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 13
 ccagcctcat ctcctttctt gc

22

<210> 14
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 14
 tcacagtttc acaaacccca gg

22

<210> 15
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Primer

<400> 15
 aaacagaaga agcagcactc tg

22

54
 1

<210> 16
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 16
tcacagtttc acaaacccca gg

22

247

